February 25, 2000 1701 '00 FEB 29 P1:34

Dockets Management Branch
Food and Drug Administration
5630 Fishers Lane (HFA-305)
Room 1061
Rockville, Maryland 20852

Re: Comments to FDA Docket No. 98D-0969, "Risk Assessment on the Human Health Impact of Fluoroquinolone Resistant *Campylobacter* Associated with the Consumption of Chicken"

The following comments on the Food and Drug Administration/Center for Veterinary Medicines' *Risk Assessment on the Human Health Impact of Fluoroquinolone Resistant Campylobachter Associated with the Consumption of Chicken* are submitted on behalf of the Coalition for Animal Health. The Coalition for Animal Health represents livestock and poultry producers, veterinarians and the manufacturers of animal health products. The Coalition for Animal Health has been actively involved in the review by CVM of the potential impact on public health resulting from antibiotic use in food animals.

The nature of public comments is such that the Coalition must look most closely at areas of concern about the risk assessment. Before doing so, the Coalition would like to strongly commend CVM for its decision to conduct a risk assessment as part of the process by which it will develop an antibiotic approval and monitoring process that addresses resistance concerns. Without risk assessment, it is impossible to understand the exact nature of the threat, if any, on-farm antibiotic use poses to the development of antibiotic resistance in human medicine. CVM's decision to utilize risk assessment creates an opportunity for future agency policy to be science-based and commensurate with the real level of risk. The agency deserves tremendous credit for rejecting calls for immediate, draconian action toward on-farm antibiotic use and for listening to all stakeholders affected by CVM policy toward antibiotics.

The Coalition's appreciation of CVM's decision to embrace risk assessment does not relieve the Coalition of its obligation to point out concerns it has with the risk assessment CVM conducted last year. A close review of CVM's assessment makes it clear that the assessment, in its current form, does not provide a reasonable representation of the risk to human health posed by fluoroquinolone use in poultry. CVM's assessment model, as used in poultry, is an appropriate beginning point for the incorporation of risk assessment into the policy process. We hope that CVM will take these following comments in the constructive manner intended, so that its risk assessment can be revised and engender the full stakeholder confidence necessary to make it an effective public policy tool.

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A fundamental foundation of the CVM risk assessment is that *"the incremental human health impact of resistant food borne disease can be determined without assessing all the factors influencing the cause of disease itself"*. (page I-4) The Coalition contends that the incremental health impact cannot be determined by ignoring all other factors. In order to truly identify the incremental human health impact from fluoroquinolone use in poultry the impact of all factors potentially contributing to the development and transfer of resistant bacteria which actually produce human illness must be identified and quantified. Only at that point are you capable of isolating the component that results from the administration of antibiotics in poultry.

The failure to quantify these other factors individually essentially adds that additional level of risk to the administration of the antibiotic in poultry and will lead to misguided public policy decisions. For example, Section 5 of the model identifies a public policy action point based on the maximum prevalence of fluoroquinolone resistant *Campylobacter* on poultry meat. The assumption seems to be that once this maximum prevalence is reached restrictions would be placed on the use of the antibiotic.

Since the model design is based on the irrelevance of "assessing all factors influencing the cause of disease" a significant number of factors not considered by the model can and will influence the maximum prevalence but not be subject to policy modification. The final result of the current model structure will be as the Coalition projected during the public meeting on the Framework document. The use of antibiotics in food animals can be eliminated and no improvement in human health may result. The risk assessment seems to assume that the existence of a single campylobacter present on poultry meat at slaughter is adequate to cause infection.

In addition the model equates infection with illness. These assumptions and their use in this or a modified risk assessment model need to be reevaluated. Prevalence of campylobacter at slaughter is not an adequate proxy for prevalence after refrigeration and cooking. And just as importantly the number of cells present at the time of consumption must be of a sufficient number to cause actual illness. The variation in individual responses to the presence of campylobacter must also be accounted for to determine the true incidence of illness. The risk assessment model on campylobacter and fluoroquinolones recently completed (but not yet published) by the Georgetown University Center for Food Policy more explicitly incorporates direct estimates of cooking and consumption patterns and individual responses to campylobacter. We believe that CVM should carefully consider the methodology developed by Georgetown University and its incorporation into the CVM model.

The assumptions (Appendix C) utilized in the design of the risk assessment model are clearly set forth. In many cases the assumptions should be modified to reflect better data sources which are available and in other cases the inadequacy of the assumptions underscore the failure of the risk assessment to adequately model the variety of factors influencing illness resulting from resistant foodborne pathogens. The Coalition would like to provide comments on several of the key assumptions.

Priority 1

Assumption: *The flouroquinolone resistance observed in persons ill from campylobacteriosis, (after removal of travelers, those who took a flouroquinolone prior to culture and those for whom the time of taking the fluoroquinolone was unknown) is attributed to chickens.*

CVM acknowledges in the risk assessment document that other sources of campylobacter infection exist. The risk assessment chooses to ignore this. A more complete search of the literature for references that document campylobacter resistance to fluoroquinolones prior to their introduction into human medicine is appropriate. The failure to incorporate the risk associated with sources including contact with pets, untreated water and contaminated water will allow the model to justify inappropriate policy decisions.

Priority 2

Assumption: The level of risk ascertained in studies in the 1980's represents the current level of risk.

The studies cited by CVM in the risk assessment which attempt to quantify the potential exposure of an individual to resistant campylobacter as a result of the consumption of chicken appear to be seriously dated and do not reflect consumption and food preparation patterns today. Although the model description does acknowledge the limitations of this data the use of the data severely biases the risk assessment. It is clear that the efforts of USDA, meat and poultry processors and livestock and poultry producers to implement the Hazard Analysis and Critical Control Point inspection program and programs to educate consumers like FIGHT BAC™! have dramatically improved the safety of meat and poultry since the 1980's. The dependence of the model on such outdated and unrealistic data also raises the question as to the model's ability to incorporate future changes in factors that could change human exposure to resistant campylobacter. A risk assessment model capable of assisting in effective food safety and drug use policy should be able to incorporate continuing improvements in food safety including, for example, irradiation.

The Coalition recommends that in order to continue the process of determining the actual risk to human health from antibiotic use in food animals that CVM take the following actions:

1. Ask Dr. Vose to test the risk assessment model to ensure that it is statistically and mathematically consistent and produces meaningful results when alternative data is utilized.
2. Expand the risk assessment model to more directly account for all sources of risk that potentially impact human health risk from fluoroquinolone use.
3. Develop improved sections of the model to determine more realistic values for human exposure to resistant campylobacter and the response of individuals resulting from exposure to varying levels of resistant bacteria.

4. Sponsor a workshop of limited size to allow food scientists, epidemiologists, biostatisticians and risk assessment modeling experts (including Dr. Vose) to correct and improve the model methodology. Risk assessors not risk managers should determine the agenda for this workshop.

The Coalition continues to strongly support quantitative risk assessment as the appropriate public policy tool, and we again strongly commend CVM for its decision to incorporate risk assessment into the policy process."

Furthermore, the Coalition believes that sufficient data exists to conduct an assessment of the risk of flouroquinolone resistant bacteria and to subsequently identify and isolate the component of that risk attributable to flouroquinolone use in food animals.

The Coalition for Animal Health appreciates the opportunity to provide comments on the CVM risk assessment model. We continue to be committed to a risk based regulatory structure for the use of antibiotics in food animals, and look forward to working with you toward that goal.

The Coalition for Animal Health

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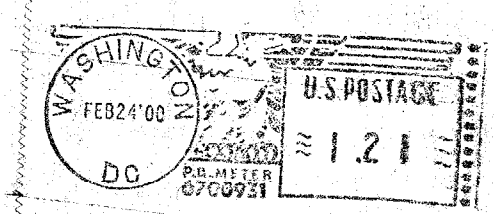

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